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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,479	MCGREGOR ET AL.	
	Examiner	Art Unit	
	Kimberly A. Makar, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *11-19 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,20-25 and 27-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 March 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/04/05; 5/07/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of invention I in the reply filed on 08/03/07 is acknowledged. The traversal is on the ground(s) that there would be no serious burden on the examiner to search all groups, and that the special technical feature of "directly or indirectly bound" is a limitation within a dependent claim, not an independent claims. In the restriction requirement dated 07/03/07 it was shown that there is no special technical feature common to the Groups and, in the absence of a unifying special technical feature, patentability of each Group must be determined based on the unique features of the Groups. Therefore, determining patentability of all of the Groups in a single application would impose a serious burden.

2. While there is no "linking claim" practice in 371 applications, as was stated in the restriction requirement of 07/03/07, "Groups I and II require the use of vector DNA constructs having mutually exclusive properties (i.e., Group I requires that the vector encode a peptide capable of binding directly to a DNA target sequence and Group II requires that the vector encode a peptide capable of binding indirectly to a DNA target sequence). Thus each Group, considered as a whole, comprises a distinct special technical feature." Thus the election of the invention was searched to the extent that the claim read on "direct binding" to a DNA target sequence. Furthermore, the elements common to the two inventions are not a contribution over the art (see *infra*) and, therefore, there is clearly no special technical feature common to the Groups. Also, the claim identified as generic to the two inventions requires a bifunctional agent (directly

binding vs. indirectly binding) and is therefore not wholly generic to the identified inventions. Determining patentability of all of the Groups in a single application would impose a serious burden.

3. Applicant's election with traverse of RepA and Ori in the reply filed on 08/03/07 is acknowledged. The traversal is on the ground(s) that there would be no serious burden on the examiner. This is not found persuasive because the encoding proteins (RepA and oestrogen receptor) and corresponding DNA target sequences between the two species are mutually exclusive. Therefore, determining patentability of all of the Groups in a single application would impose a serious burden.

The requirement is still deemed proper and is therefore made FINAL.

4. Claim 11—19 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/03/07.

Drawings

5. The drawings are objected to under 37 CFR 1.83(a) because they fail to show details as described in the specification. Specifically, drawings 6, 8, and 9 all comprise multiple bar graphs representing the results of multiple experiments. However, there are multiple columns without shading, and therefore one is unable to determine from the graph, the figure legend or the description of the drawings in the specification which column refers to which specific experimental data set. Any structural detail that is

essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

6. Claim 10 is objected to because of the following informalities: claim 10 is not grammatically correct. The claim recites "a method according to claim 1 wherein DNA not bound by the peptide encoded by said DNA of (iii) is bound by non-specific binding

protein". Should the phrase be "is bound by a non-specific protein" or "is bound by non-specific proteins?" Appropriate correction is required.

7. Claim 5 is objected to as not being grammatically correct. Claim 5 recites the phrase, "wherein sid DNA target sequence of (i) is ori." This phrase is missing an article: "is an ori" or "is an origin of replication" or "is an origin of replication that is recognized by RepA." Appropriate correction is required.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 2, 4, 6,10, 20-24, 27-32, and 34-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Schatz et al (US Patent 6,156,511) (of record 07/03/07). Claims 1, 2, 4, 6,10, 20-22, 24, 27-31, 34-40, 43-44 read on a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides encoding antibodies or fragments thereof, wherein each peptide is linked to the DNA construct encoding the peptide, comprising the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA

constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced. The method further comprises wherein said DNA construct further comprises: (iv) a DNA element that directs cis-activity; wherein the peptide encoded by said DNA of (iii) is capable of recognizing and directly binding said DNA target sequence of (i); wherein the DNA is constructed by restriction enzyme digestion and ligation. The method is further limited wherein DNA not bound by the peptide encoded by said DNA of (iii) is bound by a non-specific DNA binding protein, and is under the control of suitable promoter and translation sequences to allow for in vitro transcription and translation and is carried out in a coupled bacterial transcription/translation environment.

10. The claims also read on a method of using the library to screen for ligand binding proteins, and DNA binding proteins wherein the target sequence peptides are zinc finger proteins, helix-loop-helix proteins or helix-turn-helix proteins. The claims are also directed towards the DNA constructs and vectors encoding the library peptides, host cells expressing the DNA constructs for the recited methods, an that the methods are performed in the presence of a compound which inhibits nuclease activity, or reduced non-specific DNA-protein or protein-protein interactions.

11. Schatz et al (US Patent 6,156,511) teaches methods of making and using a library, wherein the vector includes the DNA domain in which the DNA-binding protein binds to (ie encodes a target sequence). The interaction between the DNA binding

protein and DNA is non-covalent, and is affect by such parameters as temperature, pH, ionic strength, etc (column 13, lines 45-65).

12. Schatz teaches:

"the peptide library is constructed so that the DNA binding protein can bind to the recombinant DNA expression vector that encodes the fusion product of interest. The method of generating the peptide library of the invention comprises the steps of (a) constructing a recombinant DNA vector that encodes a DNA binding protein and contains a binding site for he DNA binding protein; (b) inserting into the coding sequence of the DNA binding protein in the vector of step (a) a coding sequence for a peptide such that the resulting vector encodes a fusion protein comprises the DNA binding protein and the peptide; (c) transforming a host cell with the vector of step (b) and (d) culturing the host cell transformed in step (c) under conditions suitable for expression of the fusion protein (column 2, lines 41-55).

13. A specific embodiment includes the lac repressor operons, which bind the lac repressor proteins, which are fused to a peptide of interest of the library (see figure 1). The vector binds to the expressed peptide that it encoded.

14. He teaches that suitable DNA binding proteins include proteins with known DNA binding domains, such as those with helix-turn-helix, helix-loop-helix and zinc finger proteins (column 7, lines 4-45), and that the protein to be expressed for fusion to the DNA binding domain, the members of the library include antibodies and fragments there of (column 5, lines 23-33; column 22, line 40 - column 23 line 5). He teaches that the vectors expressing the DNA and DNA-binding protein libraries are expressed in host cells such as e coli (which reads on a bacterial transcription/translation environment), and that the peptide library contains at least 10^6 different members (column 6, lines 47-49; column 11 lines 11).

15. The present specification teaches "cis activity":

16. In some cases, cis activity may be provided due to the presence of a DNA element that directs cis-activity. i.e. that allows or forces the protein encoded by the DNA construct to have cis-activity, and therefore to bind to its encoding sequence. In other cases, a separate DNA element per se may not be required where the nature of the encoding DNA inherently confers cis activity on the encoded peptide.

17. Schatz teaches that the DNA encoding the DNA-binding protein that binds to the DNA that encodes it comprises a spacer region 3' of the coding region of the library peptide (column 5, lines 1-11; column 9, lines 32-48; column 16, lines 49-67) which allows the DNA to bind to the DNA-binding protein. This reads on the DNA comprises CIS activity. The DNA encoding vectors are made via restriction enzymes and ligation techniques well known in the art (see examples, and column 9, lines 32-48). He teaches that the library can be screened on, and selected from, a solid support such as a streptavidin immobilized on a plastic plate, cell sorter etc. (see figure 1, and column 13, lines 30-45). Furthermore the DNA binding protein can be altered such that it binds nonspecifically to the original binding domain (column 8, lines 49-64) thus the DNA is can be bound by a non-specific DNA binding protein that still recognizes the DNA sequence. The vector is under the control of various promoters and translation sequences which allow for in vitro transcription and translation (column 8, lines 27-35, and column 11 lines 27-49). He further teaches that the library is made and screened in the presence of ice, which inherently prevents nuclease activity, and teaches that the conditions which affect stability of the non-covalent interactions (i.e. non-specific DNA-protein interactions) can be adjusted by adjusting temperature, ph, and ionic concentrations of the solution (see example 3 and column 13, lines 45-65).

18. Schatz specifically teaches that the library is used to identify antibody ligands or to identify new DNA binding proteins (column 23 line 52 – column 24 line 35). He teaches that members of the library are screened and isolated, and can be further subcloned and expressed and isolated in vitro (see column 26- lines 23-column 27 line 14 and examples).

19. Thus Schatz teaches the claimed invention.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 3, 5, 7, 8, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz et al (US Patent 6,156,511) (of record 07/03/07) as applied to claim 1 above, and further in view of Prazkeir et al (Role of CIS in Replication of an IncB Plasmid. Journal of Bacteriology, 1999. 181(9):2765-2772 (listed in applicant's IDS dated 5/27/05). Claims 3, 5, 7, 8, 9 read on a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides encoding a RepA fusion peptide, wherein each RepA peptide is linked to the DNA construct encoding the RepA peptide, comprising the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence that is an origin of replication that is recognized by RepA; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced. The method is further limited wherein repA is selected from the group consisting of repA of the Incl complex plasmids and repA of the IncF, IncB, IncK, IncZ and IncL/M plasmids and the cis DNA element and the ori DNA of the IncFII plasmid R1. The method is further limited wherein said repA protein has the sequence given in SEQ ID NO: 16 and wherein said cis DNA element has the sequence given in SEQ ID NO: 17.

23. The instant specification teaches that SEQ ID NO: 16 and 17 are isolated from the IncFII R1 plasmid (page 6, lines 30-31).

24. Schatz et al (US Patent 6,156,511) teaches a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides encoding antibodies or fragments thereof, wherein each peptide is linked to the DNA construct encoding the peptide, comprising the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced (see above).

25. Schatz further teaches that the method of making the library is malleable, and a skilled artisan can utilize the methodology to create libraries using alternate DNA binding proteins and their DNA sequences, including known DNA binding proteins including transcriptional regulators and proteins that serve structural functions on DNA anything with a helix-turn-helix motif, such as the phage 434 repressor, the lambda phage cI and cro repressors, the E. coli CAP protein from bacteria, proteins with a homeobox helix-turn-helix motif, proteins with a helix-loop-helix structure, such as myc and related proteins, proteins with leucine zippers and DNA binding basic domains such as fos and jun, proteins with `POU` domains such as the Drosophila paired protein, proteins with domains whose structures depend on metal ion chelation such as zinc fingers found in TFIIIA, or proteins such as Gal4, certain retroviral nucleocapsid

proteins, some nuclear hormone receptor-type proteins; the phage P22 Arc and Mnt repressors and proteins that bind DNA in a non-sequence-specific manner are also used, for example, histories, protamines, and HMG type proteins, as well as proteins could be used that bind to DNA indirectly, by virtue of binding another protein bound to DNA such as yeast Gal80 and adenovirus E1A protein (Column 7, lines 15-42). However, Schatz does not teach that the specific DNA-binding proteins and corresponding DNA target sequence includes the RepA and Rep Ori sequences, as encoded by SEQ ID NO:16 and SEQ ID NO:17.

26. Praskier teaches the delineation of the interaction of RepA with the ori and CIS elements of the Rep A gene (see abstract). He teaches that it is known in the art that the RepA protein interacting with its coding DNA (see introduction). Praskier teaches that the RepA protein is capable of interacting the Cis elements from the IncI, IncF, IncB, IncK and IncL/M plasmids (see Table 1, figure 3 and page 2767 2nd column, last 2 paragraphs, though page 2768 first column). He further teaches that the Rep A proteins are very highly homologous, and direct sequence homology is not required for the Rep A protein to interact with the CIS element (see page 2767 2nd column, last 2 paragraphs, though page 2768 first column). He further states that the Rep A protein, CIS and ori sequences of the Rep A gene of the plasmid IncB, are highly homologous to the plasmid vectors IncFII R1 and R100 as disclosed in the art (page 2771, column I, last paragraph). The Rep A protein and ori as identified by SEQ ID NOL 16 and SEQ ID NO:17 are encoded on the IncFII R1 plasmid (see page 6, lines 30-31 of the instant

specification). Thus the Rep A protein and Ori from the R1 plasmid encodes SEQ ID NO:16 and SEQ ID NO:17.

27. Thus Praskier, discloses that the plasmids IncI, IncF, IncB, IncK and IncL/M plasmids, and Inc FII R1 and R100 are known in the art, and expresses highly homologous Rep A proteins, and highly homologous CIS and Ori regions. He further teaches that the CIS and Ori regions of the various plasmids are capable direct interaction with the Rep A protein, and suggests all of the RepA proteins interact with the CIS and ori regions in a similar manner, and that base pair specificity is not required for such interactions (page2770-2771, see entire discussion).

28. It would have been obvious to the skilled artisan at the time the invention was made to combine the teachings of Schatz et al on a method of making and using a malleable library of various DNA-binding proteins that noncovalently bind to the DNA that encodes them with the teaching of Praskier on the ability of Rep A to directly noncovalently interact with it's CIS and Ori regions, and that the RepA proteins, CIS and Ori regions are highly homologous between well known plasmids, and are capable of exchanging CIS and ORI regions between the plasmids resulting in the maintenance of the RepA proteins of binding to the CIS and Ori region because the RepA DNA binding properties and plasmids encoding them as taught by Praskier were well known in the art at the time of the invention, and that the methods of making and using the library as taught by Schatz were well known in the art at the time of the invention, and all of he claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their

respective function, and the combination would have yielded predictable results to one or ordinary skill in the art at the time of the invention (See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007)).

29. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz et al (US Patent 6,156,511) (of record 07/03/07) as applied to claim 1 above, and further in view of Edwards et al (US Patent 5,716,780). Claims 33 read on a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides, wherein each peptide is linked to the DNA construct encoding the peptide, comprising the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence that is an origin of replication that is recognized by peptide; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced. The method is further limited wherein the method is performed in the presence of a compound that prevents nuclease activity or reduced non-specific DNA-protein or protein-protein interactions, wherein the compound is heparin.

30. Schatz et al (US Patent 6,156,511) teaches a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides, wherein each peptide is linked to the DNA construct encoding the peptide, comprising

the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence that is an origin of replication that is recognized by peptide; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced, wherein the method is performed in the presence of a compound that prevents nuclease activity or reduced non-specific DNA-protein or protein-protein interactions, by performing the protocols on ice, and by adjusting Ph, temperature, and ionic concentrations (see above). Schatz teaches that the ratio of DNA to protein is important, and that if the ratio is not ideal, the balance of binding between DNA-protein can be altered by modifying such parameters (Column 13 lines 45-65). Schatz does not teach that the specific compound is heparin.

31. Edwards et al (US Patent 5,716,780) teaches methods for making libraries that screen for DNA-binding peptides (see abstract). She teaches methods of screening the DNA binding proteins include the use of agents that including the use of heparin which is a general DNA-binding molecule "that specifically inhibit the interaction of a given DNA-binding protein with its binding sequence (cognate site)" (column 11, lines 50-63).

32. It would have been obvious to the skilled artisan to combine the teaching of Schatz et al on a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides, wherein each peptide is linked to the

DNA construct encoding the peptide, comprising the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence that is an origin of replication that is recognized by peptide; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced, wherein the method is performed in the presence of a compound that prevents nuclease activity or reduced non-specific DNA-protein or protein-protein interactions, by performing the protocols on ice, and by adjusting Ph, temperature, and ionic concentrations in order to adjust non-specific binding when the ratio of DNA to DNA-binding peptide is not ideal with the teaching of Edwards et al on a method of screening libraries for DNA binding peptides, wherein heparin is used as a molecule that specifically inhibits the interaction of a specific binding protein with its binding sequence as it is a general DNA binding molecule, which would bind to nonspecific nucleic acids, as well as any excess of DNA vectors, thus adding another method to the method taught by Schatz on controlling the stoichiometry of the library members. All of the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one

of ordinary skill in the art at the time of the invention ((See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)).

33. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz et al (US Patent 6,156,511) (of record 07/03/07) as applied to claim 1 above, and Szostak et al (US Patent 6,281,344) further in view of Mattheakis et al (An in vitro polysome display system for identifying ligands from very large peptide libraries. PNAS, 1994.91:9022-9026) (listed in applicant's IDS dated 05/27/05). Claim 25 reads on a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides, wherein each peptide is linked to the DNA construct encoding the peptide, comprising the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence that is an origin of replication that is recognized by the peptide; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced. The method is further limited wherein the process is carried out in the S30 extract system.

34. Schatz et al (US Patent 6,156,511) teaches a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides, wherein each peptide is linked to the DNA construct encoding the peptide, comprising

the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence that is an origin of replication that is recognized by peptide; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced, wherein the method is performed in a bacterial host cell, this reading on a "bacterial transcription/translation environment. Schatz teaches his library can be used to screen for ligands, such as antibodies, or DNA binding proteins (see above). Schatz does not teach that the coupled bacterial transcription/translation environment is the S30 extract system.

35. Szostak et al teaches methods of making and screening nucleic acid/DNA binding protein libraries (libraries of DNA and DNA-binding proteins) (see abstract and introduction. Szostak specifically uses the S30 translation/transcription system in his methodology (see column 19, lines 30-51).

36. Mattheakis et al teaches the production of in vitro peptide libraries displayed on polysome using the E. coli S30 coupled transcription/translation system (see abstract). Mattheakis teaches that the library is used to screen for novel ligands (see page 9022). The method screens a nucleic acid/ribosomes complex intact on an immobilized receptor (see figure 1), thus this system is capable of transcribing and translating complexes comprising nucleic acids and proteins. Mattheakis teaches "we chose the E.

coli S30 system for in vitro expression because it translated mRNA with high efficiency, is well characterized, and is a coupled system that supports both transcription and translation" (page 9023, second column, results section).

37. It would have been obvious to the skilled artisan to combine the teaching of Schatz et al on a method for producing an in vitro peptide expression library of at least 10^4 molecules comprising a plurality of peptides, wherein each peptide is linked to the DNA construct encoding the peptide, comprising the steps of: (a) providing a DNA construct comprising: (i) a DNA target sequence that is an origin of replication that is recognized by peptide; (ii) DNA encoding a library member peptide; and (iii) DNA encoding a peptide capable of non-covalently binding directly or indirectly to said DNA target sequence of (i); wherein said DNA construct and encoded protein are selected to have cis-activity; and (b) expressing a plurality of DNA constructs according to (a) wherein said DNA constructs encode a plurality of library member peptides such that each expressed peptide is non-covalently linked to the DNA from which it was produced, wherein the method is performed in a bacterial host cell further with the teaching of Szostak on methods of making and screening nucleic acid/DNA binding protein libraries that uses the S30 translation/transcription system in his methodology further with the teaching of Mattheakis the E. coli S30 coupled transcription/translation system is a high efficiency, well characterized, and capable of transcribing and translating peptide libraries comprising nucleic acid and peptide complexes because the S30 system was well known in the art, and has been used to generate and screen libraries of nucleic acid and protein complexes for both ligands and DNA-binding

proteins. All of the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one of ordinary skill in the art at the time of the invention ((See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)).

Conclusion

38. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Kam/09/26/07

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